



# **Armed Forces College of Medicine**

## **AFCM**



# **HEPATITIS VIRUSES (Part 2)**

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**By the end of this lecture the student will be able to :**

1. Describe the structure of hepatitis viruses
2. Describe pathogenesis & clinical manifestations of hepatitis viruses
3. Describe laboratory diagnosis of hepatitis viruses
4. Outline prevention of hepatitis viruses

# Parenterally Transmitted Hepatitis Viruses



## Laboratory diagnosis of HBV

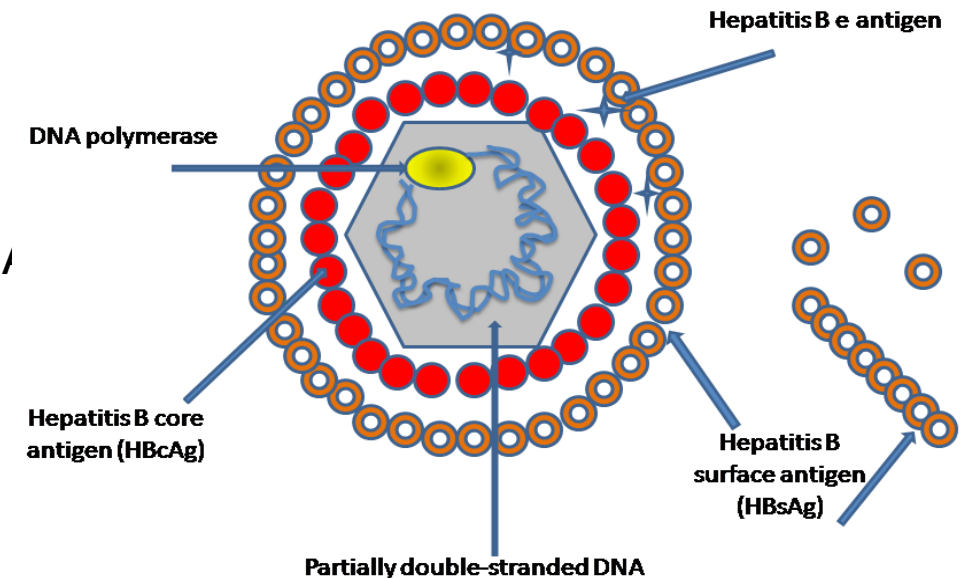
### I-Non specific tests : Liver functions tests

Marked ↑ in serum bilirubin & liver transaminases e.g ALT (alanine aminotransferase )

### II-Specific tests

A-Hepatitis B panel in serum : Detection of HBV Ags & /

B-PCR : Detection of viral DNA in blood



# Parenterally Transmitted Hepatitis Viruses



## A-Hepatitis B panel in serum : HBV markers

Detection of **HB Ags (s, & e )** &  
HB Abs (**sAb,cAb&eAb**) by ELISA

### 1-HBsAg

a. Time of detection (TOD):

Incubation period

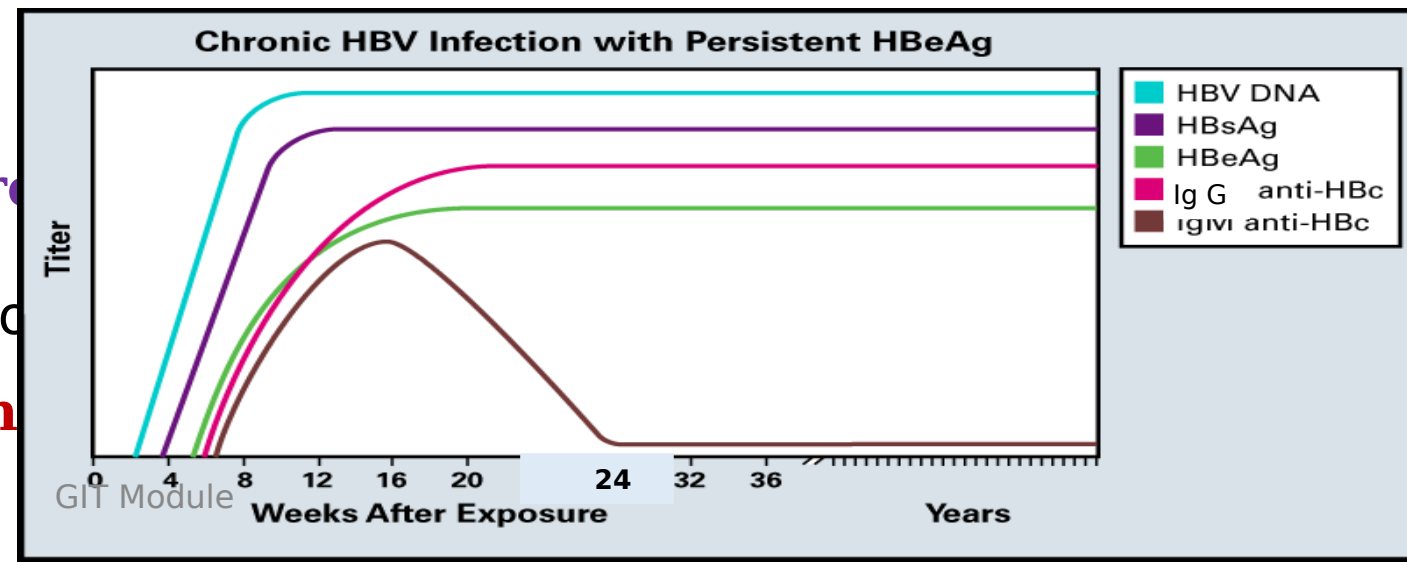
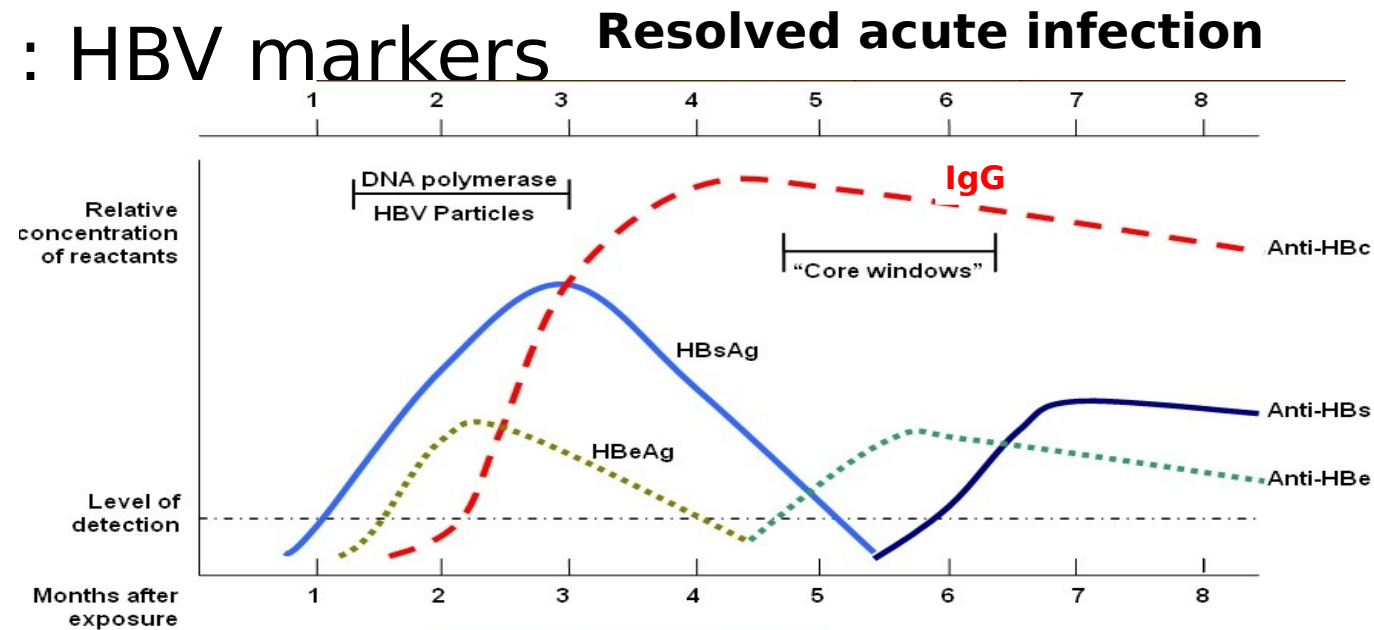


Disappears after **6 ms** except in **chronic**

b. Significance

**Acute** infection

**Chronic** infection



# Parenterally Transmitted Hepatitis Viruses



## 2-HBsAb

### a. Formation

They are made early & are **protective**

Bind to large amount of sAg

(either on Dane particles Or spherical and filamentous for  
for **neutralization** forming Ag-Ab complexes

Detected free after disappearance of sAg

b.TOD : after disappearance of sAg

**remain**

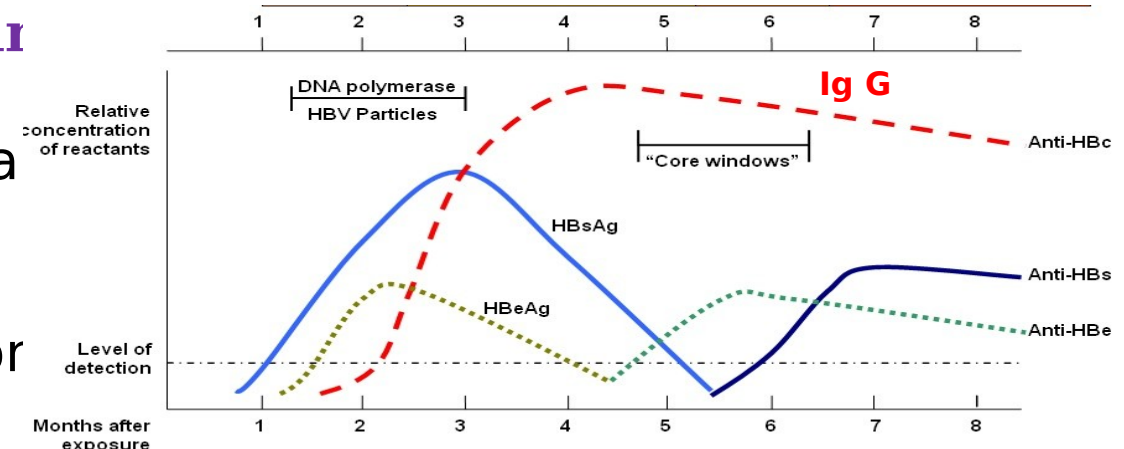
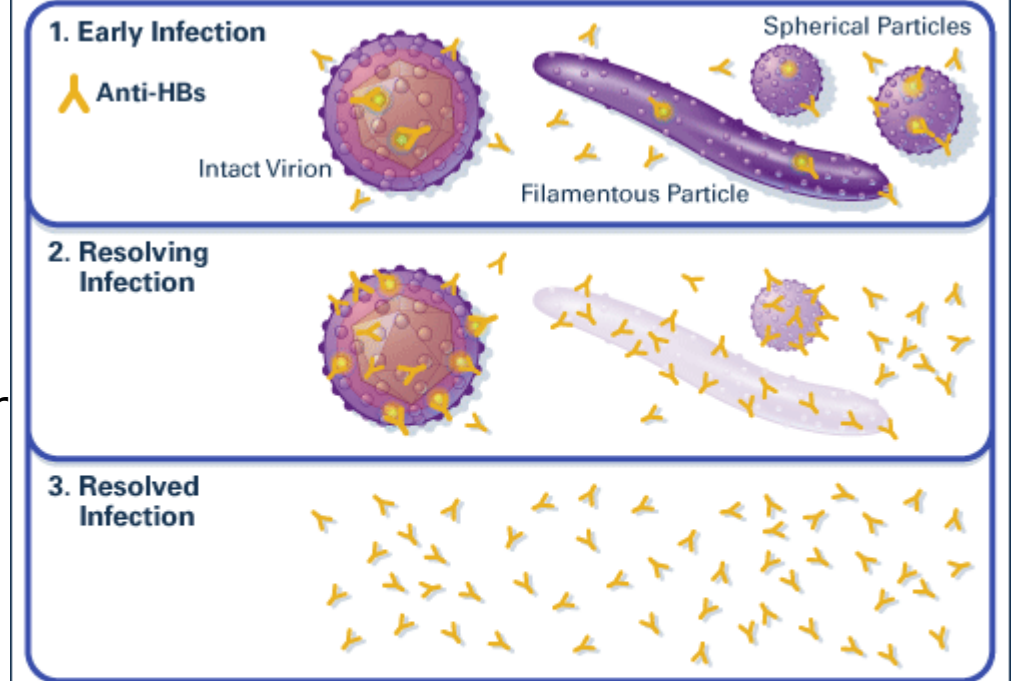
c.Sig.

**Recovery** from infection (conva

**Immunity** against reinfection

GIT Module

## Antibody to Hepatitis B Surface Antigen (Anti-HBs)



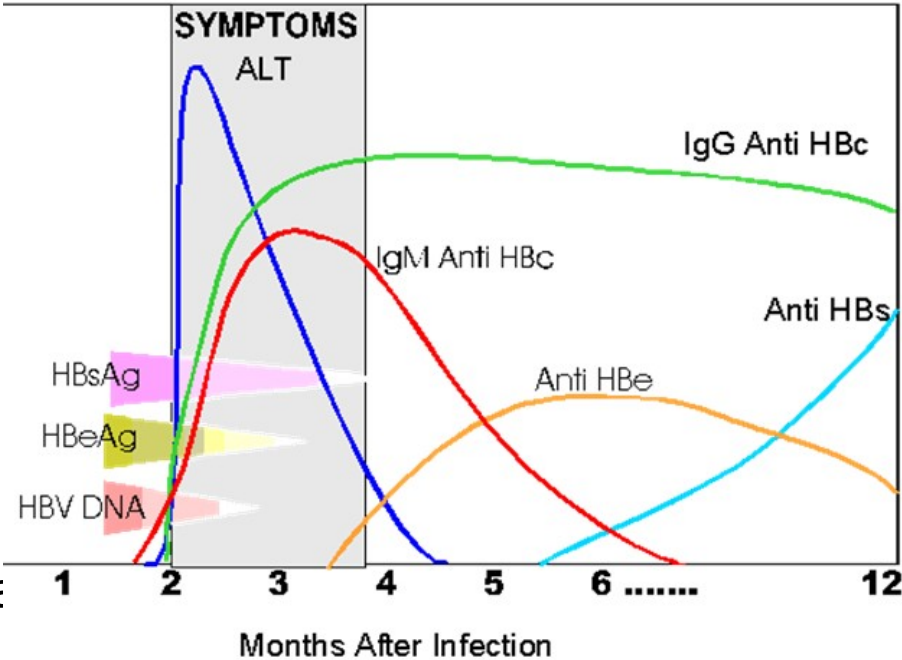
3-HBcAg

Detected only in hepatocytes ( not in serum) by liver biopsy.

4-HBcAb

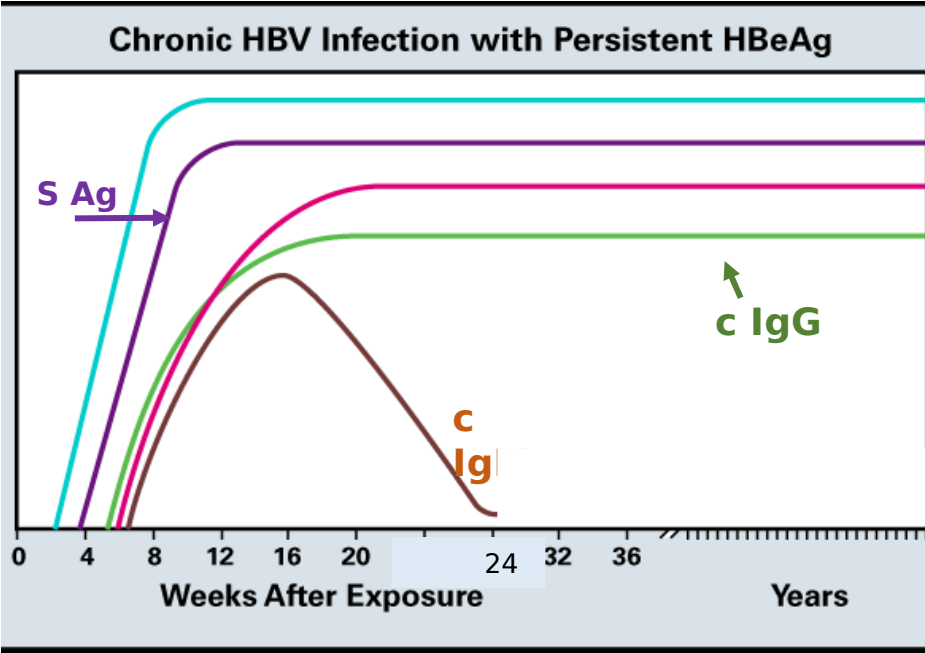
a.Formation

- Are made **early** → can be detected early **even in the presence**
- ( they **aren't protective** as cAg is inside the virus & Abs can't interact)
- Are the **best markers for viral exposure.**



	b -Time of detection	c-Significance	
<b>IgM</b>	detected at <b>clinical onset</b>	<b>Acute</b> infection ( with sAg).	<b>Window</b> phase ( without sAg)

<b>Ig G</b>	Replaces IgM completely after 6 ms  Remains for life	Chronic infection (with sAg)	Past <b>infection</b> (without sAg)  GIT Module
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# Parenterally Transmitted Hepatitis Viruses



Window phase ( in some patients)

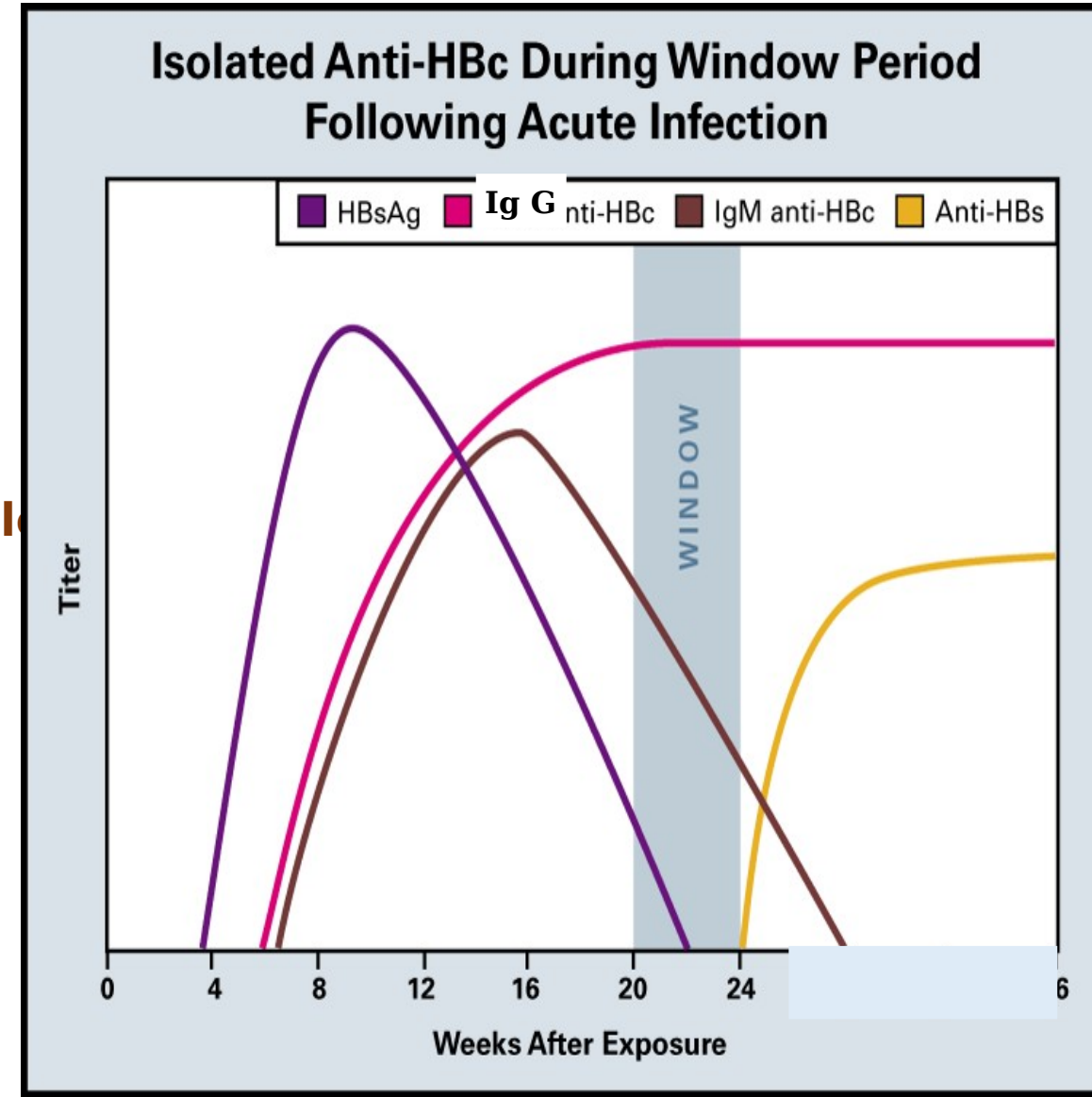
Definition

A period of several weeks during which

**sAg has disappeared** but **sAb isn't yet detectable**

Diagnosis

**HBc IgM** indicates a recent 1ry infection





# Parenterally Transmitted Hepatitis Viruses



## 5-HBeAg

a. Time of detection

Late in IP



Throughout the acute disease

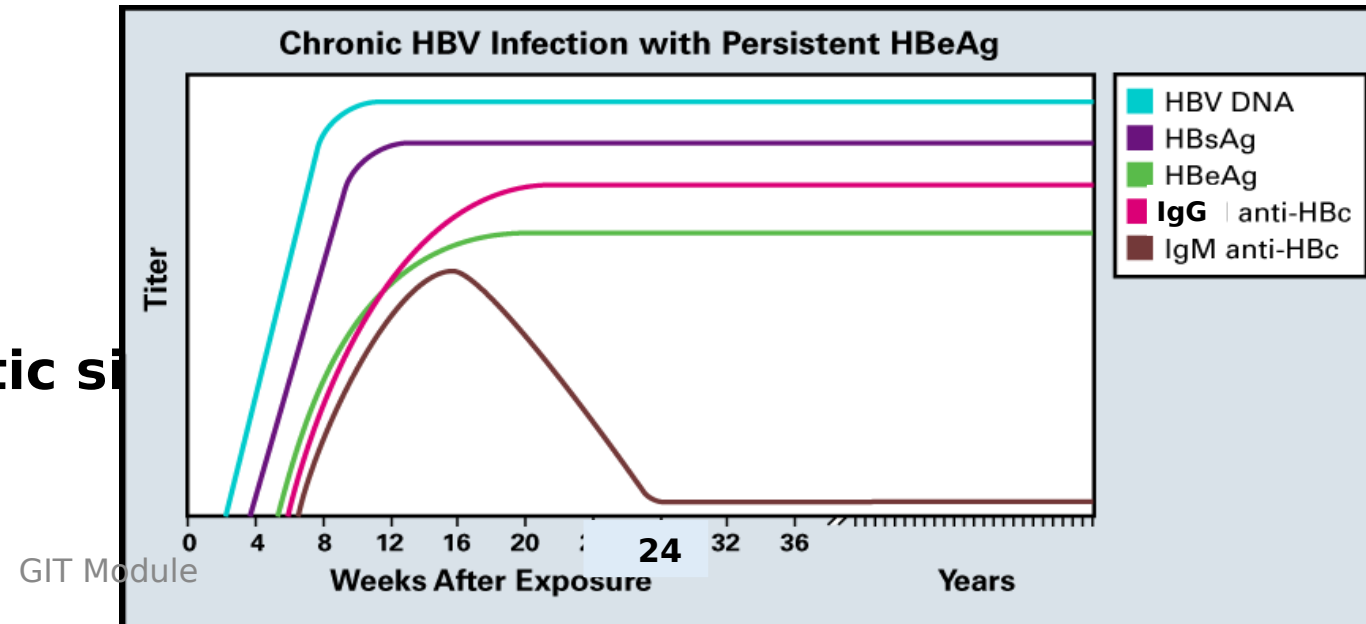
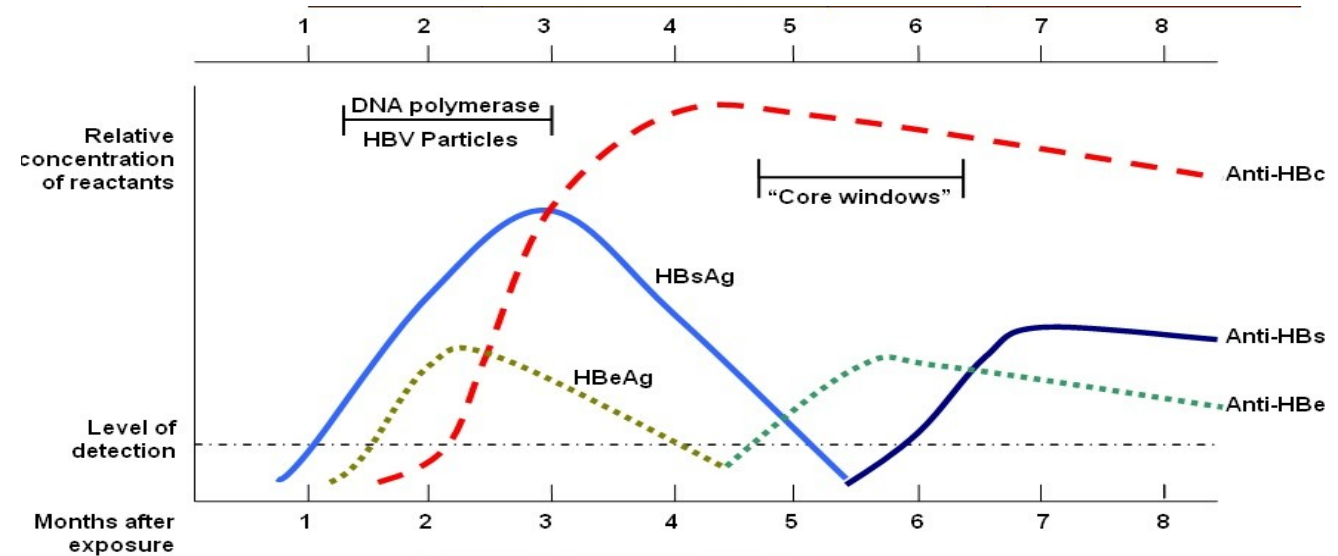


Persists in some chronic patients

b. Significance

High infectivity of patient

(its disappearance is a **good prognostic sign**)



# QUIZ



**3-HBV markers performed for a doctor following a needle stick injury were as follows: HbsAg is +ve, AntiHB c IgM is +ve ,and anti HBs Ab is -ve.**

**This doctor is probably:**

- a. A chronic carrier for HBV.
- b. Immune due to vaccination.
- c. Immune due to previous infection.
- d. Susceptible to infection by HBV.
- e. Infected with HBV in the acute stage

**e**

# HBV Panel interpretation

Test				Interpretation
HBs Ag	HBcIg M	HBcIgG	HBsAb	
1.+ve	+ve	+ve/-ve	-ve	
2.+ve	-ve	+ve	-ve	
3.-ve	+ve	+ve/-ve	-ve	
4.-ve	-ve	+ve	+ve	
5.-ve	-ve	-ve	+ve	
6.-ve	-ve	-ve	-ve	

**Choose the suitable interpretation**

**for each panel of test**

- Window phase
- Immune person due to vaccination
- Chronic infection
- Susceptible individual to infection
- Immune person due to previous infection
- Acute infection

## B- PCR : Detection of HB DNA in blood

Indicates viral replication

Need

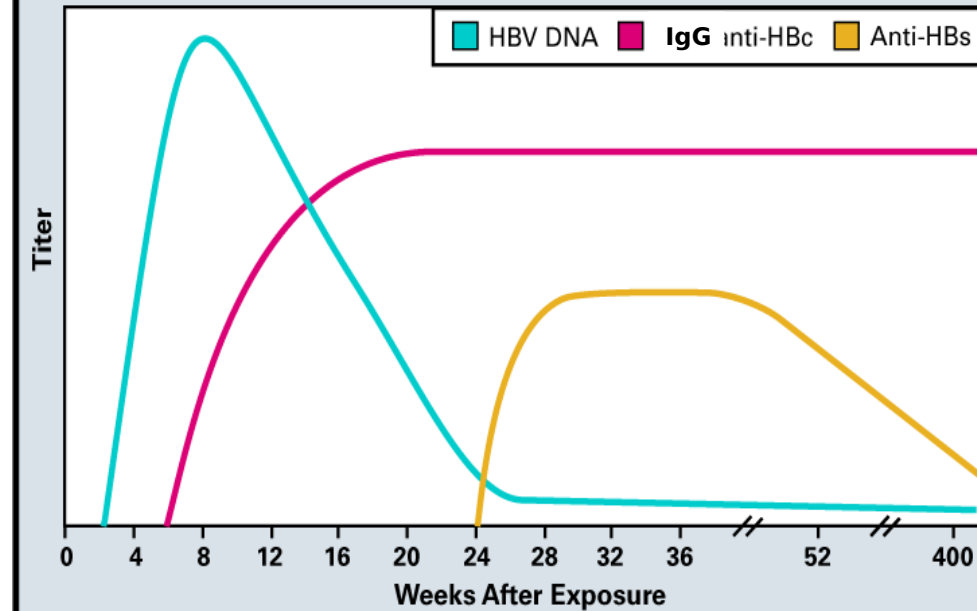
Monitor success of treatment by Quantitative

PCR

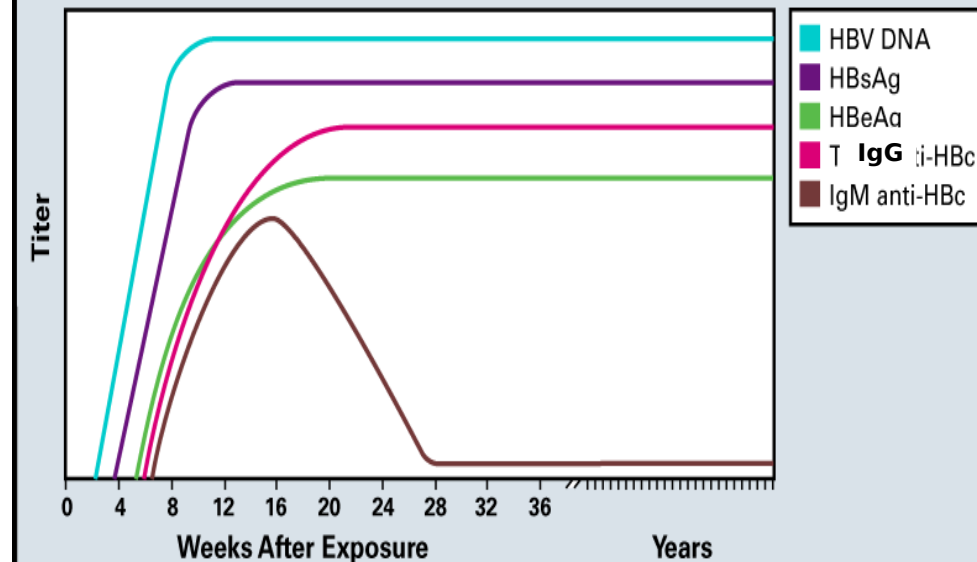
↓ viral load in patients with chronic

□ PCR doesn't differentiate hepatitis between acute & chronic infection

Resolved HBV Infection with Waning Anti-HBs



Chronic HBV Infection with Persistent HBeAg



# Parenterally Transmitted Hepatitis Viruses



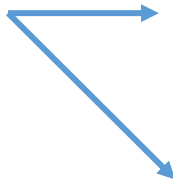
## Laboratory diagnosis of HCV

### I-Non specific tests : Liver functions tests

Marked ↑ in serum bilirubin & liver transaminases e.g ALT (alanine aminotransferase )

### II-Specific tests

#### A-Detection of Abs



#### **Rapid Ab detection test : screening test for Ab**

(false +ve result may occur due to cross reacting Abs)

#### **2<sup>nd</sup> confirmatory Ab assay**

#### B-PCR

Detection of viral RNA in blood



Current infection

# Parenterally Transmitted Hepatitis Viruses



## Scheme for diagnosis

### Rapid Ab detection test

Doesn't differentiate  
between

Current (acute or chronic)  
inf.

or resolved (cured or past)  
inf.

or False +ve (no infection)

← - - + ve

-ve

No infection

### RT-PCR

+ve

Current infection

(Active viral replication)

either

Monitor success of treatment by  
Quantitative PCR

Need  
for treatment

-ve

No current  
infection

### 2<sup>nd</sup> Ab confirmatory test

+ve

Cured (past)  
infection

-ve

False +ve rapid test  
(No infection)

↓ viral load in pts. with chronic hepatitis

# Parenterally Transmitted Hepatitis Viruses



## Hepatitis D virus (HDV, Delta virus)

A defective virus

Can't replicate by itself as it lacks gene coding for its envelope protein

Replicates only in cells **coinfected with HBV** (helper virus)

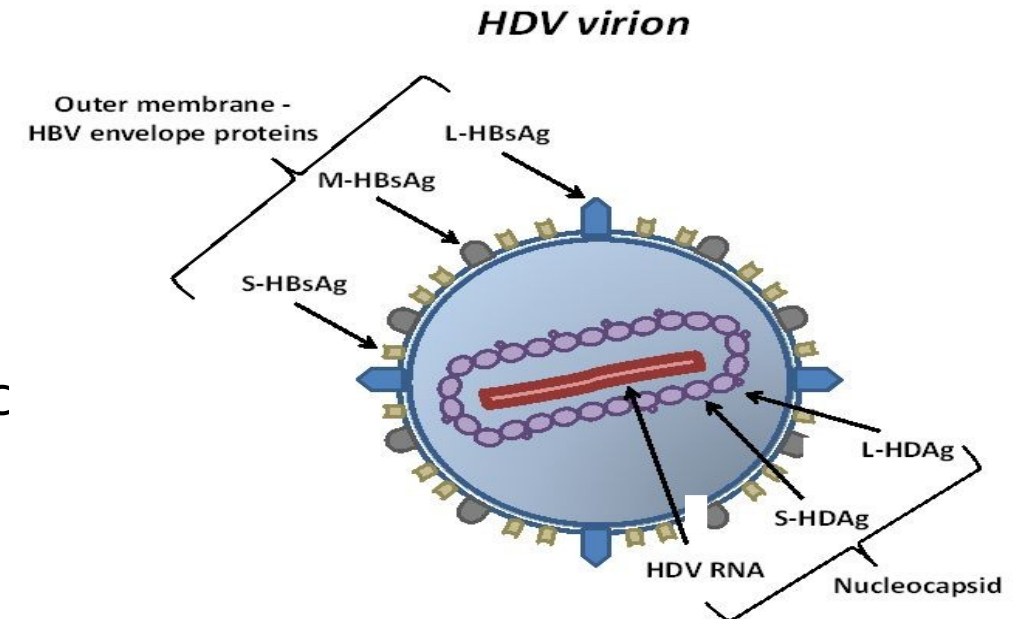
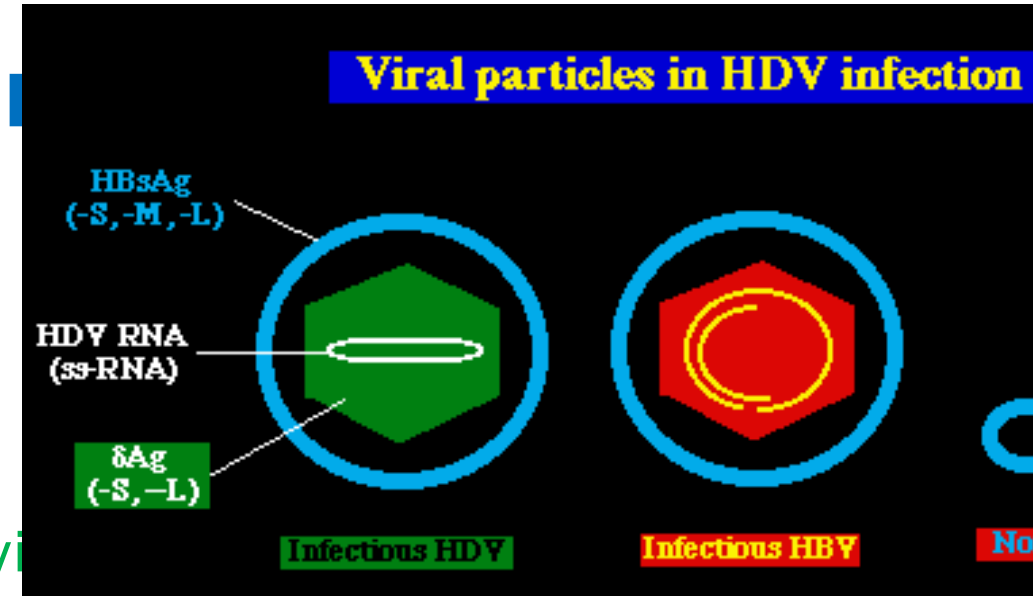
HDV uses **HBsAg** as its envelope protein

### Structure

A-Nucleocapsid → ss RNA

B-Envelope : carries **sAg**

**Delta (D)Ag** : internal c





# Parenterally Transmitted Hepatitis Viruses



## Pathogenesis

A-Entry & Spread : as HBV

B-Effect : ↑ severity of HBV infection

Coinfection of HDV

with HBV



↑ rate of

fulminant hepatitis

Superinfection with HDV

on top of HBV

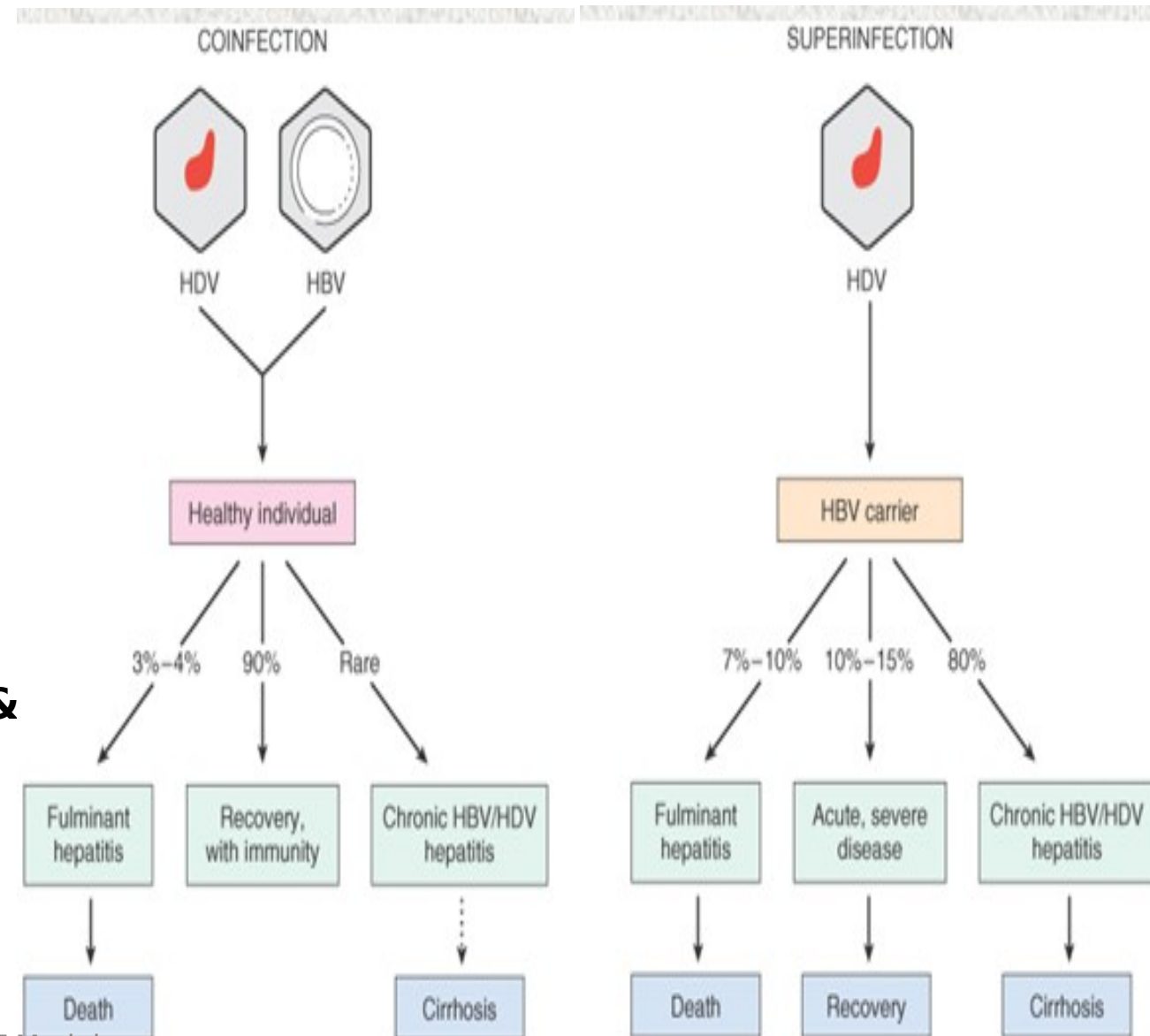


↑ rate of fulminant hepatitis &

↑ rate & severity of chronic hepatitis



↑ risk of cirrhosis,



# Parenterally Transmitted Hepatitis Viruses



## Laboratory diagnosis

**1-ELISA** → Detection of **Delta Ag**  
→ Detection of **IgM or IgG to Delta**

**2-PCR** : Detection of viral RNA

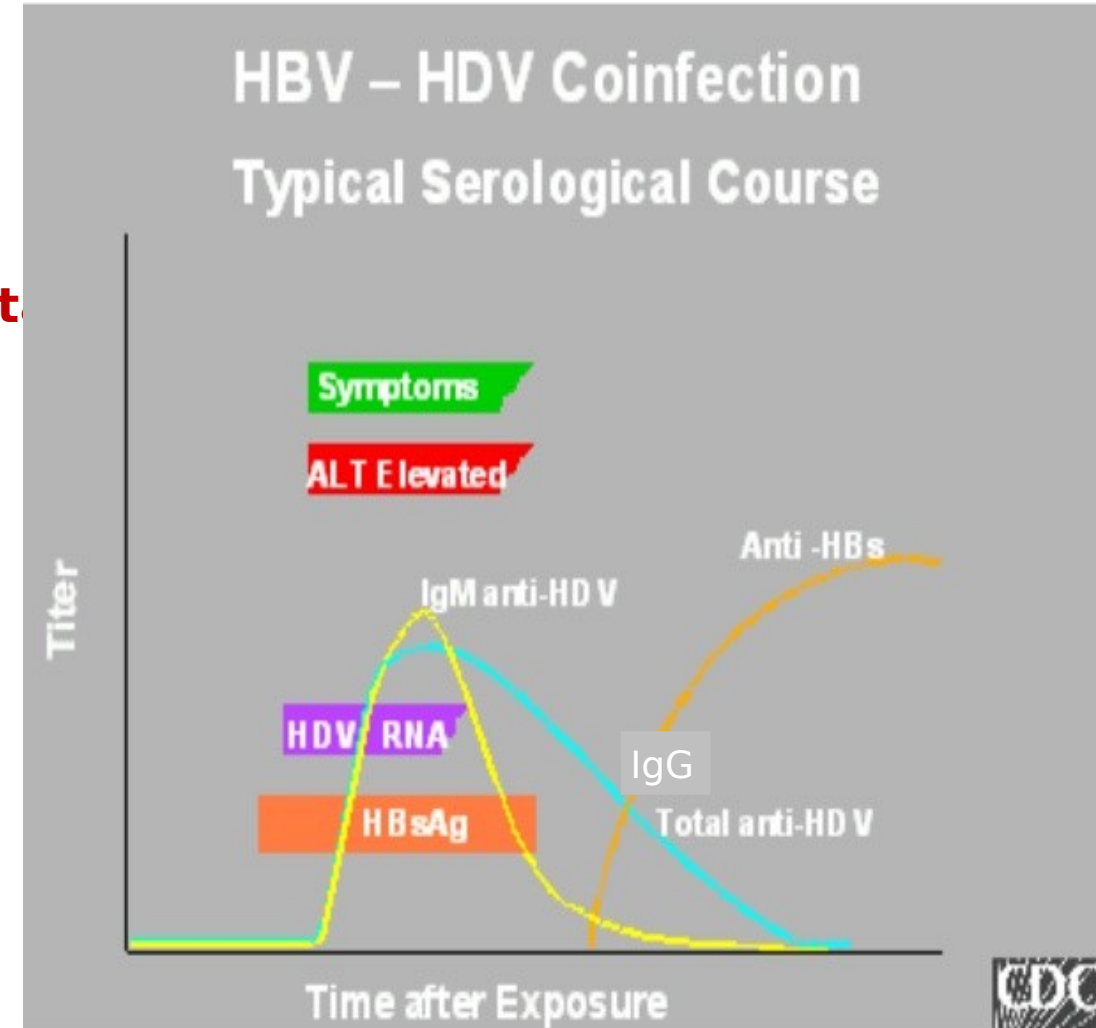
## Prevention

1-HBV vaccine prevents HDV coinfection

(HDV can't replicate unless HBV infection occurs)

2-Standard precautions & modifications of

high risk behaviors can prevent HDV superinfection

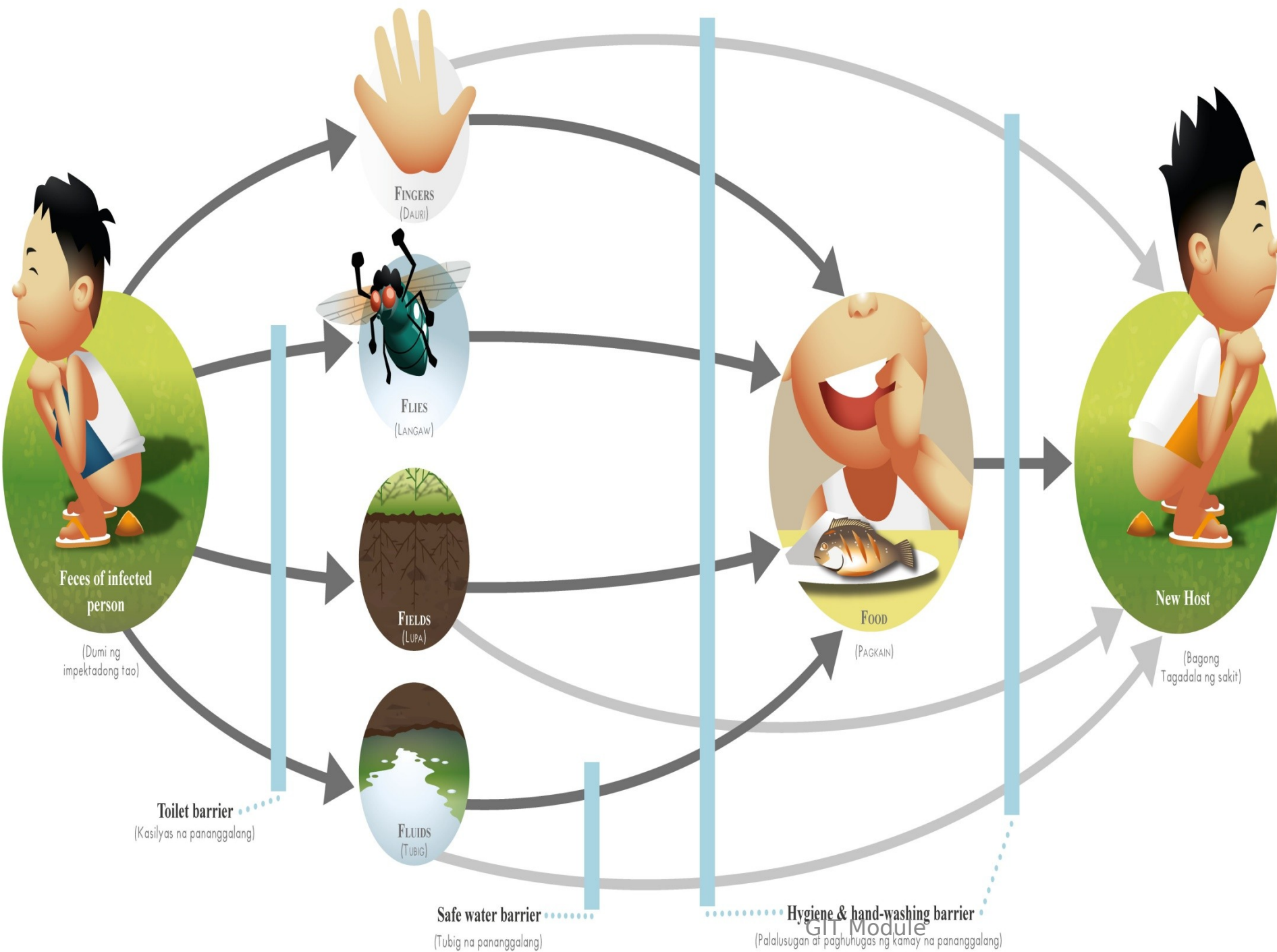


# Enterically Transmitted Hepatitis Viruses



## Hepatitis A Virus (HAV) & Hepatitis E Virus (HEV)

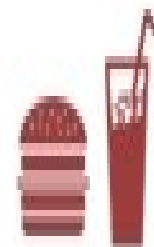
	HAV	HEV
Pathogenesis		
A - Modes of Transmission	<p>Fecal-oral : Ingestion of contaminated food &amp; water</p> <ul style="list-style-type: none"><li>● Fecally contaminated food or water can cause <b>outbreaks</b>.</li><li>● <b>Children</b> are the most frequently infected groups</li></ul> <p>† Rare transmission by blood due to low level viremia &amp; absence of chronicity</p>	



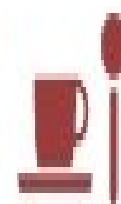
## SPREAD BY



direct  
contact



food &  
beverages



cups &  
spoons

and any other objects handled by  
the infected person

# Enterically Transmitted Hepatitis Viruses



	HAV	HEV
B-Entry & Spread	Ingestion	1 <sup>try</sup> multiplication in GIT → Spread by blood to liver
C- Effect on hepatocytes	Multiplies in hepatocytes with <b>no CPE</b> (cytopathic effect) Infected cells express viral Ags in association with MHC class I ( enhanced by interferon) → Killed by CTLs	
D-Fate of infection	1-Clearance of infection	repair of damage & recovery (in 2-4 weeks)
	2-NO : Chronicity, cirrhosis or carcinoma	High mortality (25%) in pregnant females infected in 3 <sup>rd</sup> trimester
F-Immunity	GIT Module <b>1-IgM</b> : detected at onset of jaundice	

	HAV	HEV
Clinical features		
A-Incubation period	4 weeks	
B-Symptoms & signs	<p>Most infections <b>are asymptomatic</b></p> <p>1-Fever,anorexia &amp; vomiting</p> <p>2-Jaundice,dark urine &amp; pale stools</p> <p>3-Enlarged &amp; tender liver</p>	
Laboratory diagnosis		
I-Non specific tests	As parentally transmitted hepatitis	
II-Specific tests		
<b>A-ELISA</b>	<p>Detection of Abs in serum</p> <p><b>1-IgM</b> indicates <b>recent</b> infection</p> <p><b>2-IgG</b> indicates <b>past</b> infection</p>	
<b>B-PCR</b>	Detects viral <b>RNA</b>	
Treatment	<b>No</b> antiviral drugs	

# Enterically Transmitted Hepatitis Viruses



## Prevention of HAV&HEV

### I-General hygienic measures for HAV&HEV

A-Proper hand hygiene

B-Chlorination or boiling of drinking water.

C-Proper disposal of sewage & avoiding contamination of drinking water.



# Enterically Transmitted Hepatitis Viruses



## II-Immunization for HAV

A-Active immunization : Inactivated (killed) vaccine ( Havrix)

1- Preparation : Virus **inactivated by formalin**

2-Administration : **2 doses** : 0 &6ms

3-Indications : children in endemic areas ; **2-18 years** of age

B-Passive immunization : Post-exposure prophylaxis

**HAV Igs** given **within 2 week s** after exposure



**Prevent or ↓ severity** of disease in **immunocompromised** patients

# Hepatitis viruses



## Important clinical features of hepatitis viruses

Virus	Chronic carriers	Antiviral drugs useful	Vaccine Available	Igs useful
Hepatitis A virus ( HAV)	No	No	Yes	Yes
Hepatitis B virus ( HBV)	Yes	Yes	Yes	Yes
Hepatitis C virus ( HCV)	Yes	Yes	No	No
Hepatitis D virus ( HDV)	Yes	No	No	No
Hepatitis E virus	No	No	No	No



## **Review of Medical Microbiology and Immunology.**

Warren Levinson , Thirteenth Edition.

Chapter 41 ( P 331-341).

